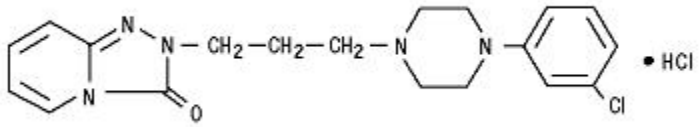
DESYREL - trazodone hydrochloride tablet
Keltman Pharmaceuticals Inc.

SUICIDALITY IN CHILDREN AND ADOLESCENTS

Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of DESYREL or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. DESYREL is not approved for use in pediatric patients. (See WARNINGS and PRECAUTIONS: Pediatric Use).
Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with major depressive disorder (MDD), obsessive compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4400 patients) have revealed a greater risk of adverse events representing suicidal thinking or behavior (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. No suicides occurred in these trials.

DESCRIPTION

DESYREL (trazodone hydrochloride) is an antidepressant chemically unrelated to tricyclic, tetracyclic, or other known antidepressant agents. Trazodone hydrochloride is a triazolopyridine derivative designated as 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1,2,4-triazolo[4,3-a]pyridin-3(2H)-one hydrochloride. It is a white, odorless, crystalline powder which is freely soluble in water. Its molecular weight is 408.3. The empirical formula is $C_{19}H_{22}ClN_5O \cdot HCl$ and the structural formula is represented as follows:



DESYREL is supplied for oral administration in 50 mg tablet.
DESYREL Tablets, 50 mg, contain the following inactive ingredients: colloidal silicon dioxide, anhydrous lactose, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate

CLINICAL PHARMACOLOGY

The mechanism of DESYREL's antidepressant action in man is not fully understood. In animals, DESYREL selectively inhibits serotonin uptake by brain synaptosomes and potentiates the behavioral changes induced by the serotonin precursor, 5-hydroxytryptophan. Cardiac conduction effects of DESYREL in the anesthetized dog are qualitatively dissimilar and quantitatively less pronounced than those seen with tricyclic antidepressants. DESYREL is not a monoamine oxidase inhibitor and, unlike amphetamine-type drugs, does not stimulate the central nervous system.

Pharmacokinetics

Absorption
In humans, DESYREL is well absorbed after oral administration without selective localization in any tissue. When DESYREL is taken shortly after ingestion of food, there may be an increase in the amount of drug absorbed, a decrease in maximum concentration and a lengthening in the time to maximum concentration. Peak plasma levels occur approximately one hour after dosing when DESYREL is taken on an empty stomach or two hours after dosing when taken with food.

Metabolism
In vitro studies in human liver microsomes show that trazodone is metabolized to an active metabolite, m-chlorophenylpiperazine (mCPP) by cytochrome P450 3A4 (CYP3A4). Other metabolic pathways that may be involved in metabolism of trazodone have not been well characterized.

Elimination
In some patients, DESYREL may accumulate in the plasma.

Drug-Drug Interactions

See also **PRECAUTIONS: Drug Interactions**. *In vitro* drug metabolism studies reveal that trazodone is a substrate of the cytochrome P450 3A4 (CYP3A4) enzyme and trazodone metabolism can be inhibited by the CYP3A4 inhibitors ketoconazole, ritonavir, and indinavir. The effect of short-term administration of ritonavir (200 mg twice daily, 4 doses) on the pharmacokinetics of a single dose of trazodone (50 mg) has been studied in 10 healthy subjects. The C_{max} of trazodone increased by 34%, the AUC

increased 2.4-fold, the half-life increased by 2.2-fold, and the clearance decreased by 52%. Adverse effects including nausea, hypotension, and syncope were observed when ritonavir and trazodone were co-administered.
Carbamazepine induces CYP3A4. Following co-administration of carbamazepine 400 mg/day with trazodone 100 mg to 300 mg daily, carbamazepine reduced plasma concentrations of trazodone (as well as mCPP) by 76% and 60%, respectively, compared to pre-carbamazepine values.
For those patients who responded to DESYREL, one-third of the inpatients and one-half of the outpatients had a significant therapeutic response by the end of the first week of treatment. Three-fourths of all responders demonstrated a significant therapeutic effect by the end of the second week. One-fourth of responders required 2 to 4 weeks for a significant therapeutic response.

INDICATIONS AND USAGE

DESYREL is indicated for the treatment of depression. The efficacy of DESYREL has been demonstrated in both inpatient and outpatient settings and for depressed patients with and without prominent anxiety. The depressive illness of patients studied corresponds to the Major Depressive Episode criteria of the American Psychiatric Association's Diagnostic and Statistical Manual, III.[1]
Major Depressive Episode implies a prominent and relatively persistent (nearly every day for at least two weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least four of the following eight symptoms: change in appetite, change in sleep, psychomotor agitation or retardation, loss of interest in usual activities or decrease in sexual drive, increased fatigability, feelings of guilt or worthlessness, slowed thinking or impaired concentration, and suicidal ideation or attempts.

CONTRAINDICATIONS

DESYREL is contraindicated in patients hypersensitive to DESYREL.

WARNINGS

Clinical Worsening and Suicide Risk

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients. Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders.
Pooled analyses of short-term placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with MDD, OCD, or other psychiatric disorders (a total of 24 trials involving over 4400 patients) have revealed a greater risk of adverse events representing suicidal behavior or thinking (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. There was considerable variation in risk among drugs, but a tendency toward an increase for almost all drugs studied. The risk of suicidality was most consistently observed in the MDD trials, but there were signals of risk arising from some trials in other psychiatric indications (obsessive compulsive disorder and social anxiety disorder) as well. **No suicides occurred in any of these trials**. It is unknown whether the suicidality risk in pediatric patients extends to longer-term use, ie, beyond several months. It is also unknown whether the suicidality risk extends to adults.
All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Such observation would generally include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks of treatment, then every other week visits for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks. Additional contact by telephone may be appropriate between face-to-face visits.
Adults with MDD or co-morbid depression in the setting of other psychiatric illness being treated with antidepressants should be observed similarly for clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.
The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.
Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.
Families and caregivers of pediatric patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence

of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for DESYREL should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. Families and caregivers of adults being treated for depression should be similarly advised.

Screening Patients for Bipolar Disorder

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that DESYREL is not approved for use in treating bipolar depression.

TRAZODONE HAS BEEN ASSOCIATED WITH THE OCCURRENCE OF PRIAPISM. IN MANY OF THE CASES REPORTED, SURGICAL INTERVENTION WAS REQUIRED AND, IN A SOME OF THESE CASES, PERMANENT IMPAIRMENT OF ERECTILE FUNCTION OR IMPOTENCE RESULTED. MALE PATIENTS WITH PROLONGED OR INAPPROPRIATE ERECTIONS SHOULD IMMEDIATELY DISCONTINUE THE DRUG AND CONSULT THEIR PHYSICIAN.

The detumescence of priapism and drug-induced penile erections has been accomplished by both pharmacologic, eg, the intracavernosal injection of alpha-adrenergic stimulants such as epinephrine and norepinephrine, as well as surgical procedures.[2-7] Any pharmacologic or surgical procedure utilized in the treatment of priapism should be performed under the supervision of a urologist or a physician familiar with the procedure and should not be initiated without urologic consultation if the priapism has persisted for more than 24 hours.

DESYREL (trazodone hydrochloride) is not recommended for use during the initial recovery phase of myocardial infarction. Caution should be used when administering DESYREL to patients with cardiac disease, and such patients should be closely monitored, since antidepressant drugs (including DESYREL) have been associated with the occurrence of cardiac arrhythmias. Recent clinical studies in patients with pre-existing cardiac disease indicate that DESYREL may be arrhythmogenic in some patients in that population. Arrhythmias identified include isolated PVCs, ventricular couplets, and in two patients, short episodes (3–4 beats) of ventricular tachycardia.

PRECAUTIONS

General

The possibility of suicide in seriously depressed patients is inherent in the illness and may persist until significant remission occurs. Therefore, prescriptions should be written for the smallest number of tablets consistent with good patient management.

Hypotension, including orthostatic hypotension and syncope, has been reported to occur in patients receiving DESYREL. Concomitant administration of antihypertensive therapy with DESYREL may require a reduction in the dose of the antihypertensive drug.

Little is known about the interaction between DESYREL and general anesthetics; therefore, prior to elective surgery, DESYREL should be discontinued for as long as clinically feasible.

As with all antidepressants, the use of DESYREL should be based on the consideration of the physician that the expected benefits of therapy outweigh potential risk factors.

Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with DESYREL and should counsel them in its appropriate use. A patient Medication Guide About Using Antidepressants in Children and Teenagers is available for DESYREL. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking DESYREL.

Clinical Worsening and Suicide Risk

Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to observe for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may

be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

Because priapism has been reported to occur in patients receiving DESYREL, patients with prolonged or inappropriate penile erection should immediately discontinue the drug and consult with the physician (see **WARNINGS**).

Antidepressants may impair the mental and/or physical ability required for the performance of potentially hazardous tasks, such as operating an automobile or machinery; the patient should be cautioned accordingly.

DESYREL may enhance the response to alcohol, barbiturates, and other CNS depressants.

DESYREL should be given shortly after a meal or light snack. Within any individual patient, total drug absorption may be up to 20% higher when the drug is taken with food rather than on an empty stomach. The risk of dizziness/lightheadedness may increase under fasting conditions.

Laboratory Tests
Occasional low white blood cell and neutrophil counts have been noted in patients receiving DESYREL. These were not considered clinically significant and did not necessitate discontinuation of the drug; however, the drug should be discontinued in any patient whose white blood cell count or absolute neutrophil count falls below normal levels. White blood cell and differential counts are recommended for patients who develop fever and sore throat (or other signs of infection) during therapy.

Drug Interactions
In vitro drug metabolism studies suggest that there is a potential for drug interactions when trazodone is given with CYP3A4 inhibitors. Ritonavir, a potent CYP3A4 inhibitor, increased the C_{max}, AUC, and elimination half-life, and decreased clearance of trazodone after administration of ritonavir twice daily for 2 days. Adverse effects including nausea, hypotension, and syncope were observed when ritonavir and trazodone were co-administered. It is likely that ketoconazole, indinavir, and other CYP3A4 inhibitors such as itraconazole or nefazodone may lead to substantial increases in trazodone plasma concentrations, with the potential for adverse effects. If trazodone is used with a potent CYP3A4 inhibitor, a lower dose of trazodone should be considered.
Carbamazepine reduced plasma concentrations of trazodone when co-administered. Patients should be closely monitored to see if there is a need for an increased dose of trazodone when taking both drugs.
Increased serum digoxin or phenytoin levels have been reported to occur in patients receiving DESYREL concurrently with either of those two drugs.
It is not known whether interactions will occur between monoamine oxidase (MAO) inhibitors and DESYREL. Due to the absence of clinical experience, if MAO inhibitors are discontinued shortly before or are to be given concomitantly with DESYREL, therapy should be initiated cautiously with gradual increase in dosage until optimum response is achieved.

Therapeutic Interactions
Concurrent administration with electroshock therapy should be avoided because of the absence of experience in this area.
There have been reports of increased and decreased prothrombin time occurring in warfarinized patients who take DESYREL.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No drug- or dose-related occurrence of carcinogenesis was evident in rats receiving DESYREL in daily oral doses up to 300 mg/kg for 18 months.

Pregnancy Category C
DESYREL has been shown to cause increased fetal resorption and other adverse effects on the fetus in two studies using the rat when given at dose levels approximately 30 to 50 times the proposed maximum human dose. There was also an increase in congenital anomalies in one of three rabbit studies at approximately 15 to 50 times the maximum human dose. There are no adequate and well-controlled studies in pregnant women. DESYREL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
DESYREL and/or its metabolites have been found in the milk of lactating rats, suggesting that the drug may be secreted in human milk. Caution should be exercised when DESYREL is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in the pediatric population have not been established (see **BOXED WARNING** and **WARNINGS: Clinical Worsening and Suicide Risk**).
Anyone considering the use of DESYREL in a child or adolescent must balance the potential risks with the clinical need.

ADVERSE REACTIONS

Because the frequency of adverse drug effects is affected by diverse factors (eg, drug dose, method of detection, physician judgment, disease under treatment, etc.) a single meaningful estimate of adverse event incidence is difficult to obtain. This problem is illustrated by the variation in adverse event incidence observed and reported from the inpatients and outpatients treated with DESYREL. It is impossible to determine precisely what accounts for the differences observed.

Clinical Trial Reports

The table below is presented solely to indicate the relative frequency of adverse events reported in representative controlled clinical studies conducted to evaluate the safety and efficacy of DESYREL® (trazodone hydrochloride).

The figures cited cannot be used to predict precisely the incidence of untoward events in the course of usual medical practice where patient characteristics and other factors often differ from those which prevailed in the clinical trials. These incidence figures, also, cannot be compared with those obtained from other clinical studies involving related drug products and placebo as each group of drug trials is conducted under a different set of conditions.

Treatment-Emergent Symptom Incidence				
	Inpts.		Outpts.	
	D	P	D	P
Number of Patients	142	95	157	158
% of Patients Reporting				
Allergic				
Skin Condition/Edema	2.8	1.1	7.0	1.3
Autonomic				
Blurred Vision	6.3	4.2	14.7	3.8
Constipation	7.0	4.2	7.6	5.7
Dry Mouth	14.8	8.4	33.8	20.3
Cardiovascular				
Hypertension	2.1	1.1	1.3	*
Hypotension	7.0	1.1	3.8	0.0
Shortness of Breath	*	1.1	1.3	0.0
Syncope	2.8	2.1	4.5	1.3
Tachycardia/ Palpitations	0.0	0.0	7.0	7.0
CNS				
Anger/Hostility	3.5	6.3	1.3	2.5
Confusion	4.9	0.0	5.7	7.6
Decreased Concentration	2.8	2.1	1.3	0.0
Disorientation	2.1	0.0	*	0.0
Dizziness/ Lightheadedness	19.7	5.3	28.0	15.2
Drowsiness	23.9	6.3	40.8	19.6
Excitement	1.4	1.1	5.1	5.7
Fatigue	11.3	4.2	5.7	2.5
Headache	9.9	5.3	19.8	15.8
Insomnia	9.9	10.5	6.4	12.0
Impaired Memory	1.4	0.0	*	*
Nervousness	14.8	10.5	6.4	8.2
Gastrointestinal				
Abdominal/Gastric Disorder	3.5	4.2	5.7	4.4
Bad Taste in Mouth	1.4	0.0	0.0	0.0
Diarrhea	0.0	1.1	4.5	1.9

Nausea/Vomiting	9.9	1.1	12.7	9.5
Musculoskeletal				
Musculoskeletal Aches/ Pains	5.6	3.2	5.1	2.5
Neurological				
Incoordination	4.9	0.0	1.9	0.0
Paresthesia	1.4	0.0	0.0	*
Tremors	2.8	1.1	5.1	3.8
Sexual Function				
Decreased Libido	*	1.1	1.3	*
Other				
Decreased Appetite	3.5	5.3	0.0	*
Eyes Red/Tired/Itching	2.8	0.0	0.0	0.0
Head Full-Heavy	2.8	0.0	0.0	0.0
Malaise	2.8	0.0	0.0	0.0
Nasal/Sinus Congestion	2.8	0.0	5.7	3.2
Nightmares/Vivid Dreams	*	1.1	5.1	5.7
Sweating/Clamminess	1.4	1.1	*	*
Tinnitus	1.4	0.0	0.0	*
Weight Gain	1.4	0.0	4.5	1.9
Weight Loss	*	3.2	5.7	2.5

* Incidence less than 1%

D = DESYREL P = PLACEBO

Occasional sinus bradycardia has occurred in long-term studies.

In addition to the relatively common (ie, greater than 1%) untoward events enumerated above, the following adverse events have been reported to occur in association with the use of DESYREL® (trazodone hydrochloride) in the controlled clinical studies: akathisia, allergic reaction, anemia, chest pain, delayed urine flow, early menses, flatulence, hallucinations/delusions, hematuria, hypersalivation, hypomania, impaired speech, impotence, increased appetite, increased libido, increased urinary frequency, missed periods, muscle twitches, numbness, and retrograde ejaculation.

Post-Introduction Reports

Although the following adverse reactions have been reported in DESYREL users, the causal association has neither been confirmed nor refuted.

Voluntary reports received since market introduction include the following: abnormal dreams, agitation, alopecia, anxiety, aphasia, apnea, ataxia, breast enlargement or engorgement, cardiospasm, cerebrovascular accident, chills, cholestatis, clitorism, congestive heart failure, diplopia, edema, extrapyramidal symptoms, grand mal seizures, hallucinations, hemolytic anemia, hirsutism, hyperbilirubinemia, increased amylase, increased salivation, insomnia, leukocytosis, leukonychia, jaundice, lactation, liver enzyme alterations, methemoglobinemia, nausea/vomiting (most frequently), paresthesia, paranoid reaction, priapism (See **WARNINGS** and **PRECAUTIONS:Information for Patients**; some patients have required surgical intervention), pruritus, psoriasis, psychosis, rash, stupor, inappropriate ADH syndrome, tardive dyskinesia, unexplained death, urinary incontinence, urinary retention, urticaria, vasodilation, vertigo and weakness.

Cardiovascular system effects which have been reported include the following: conduction block, orthostatic hypotension and syncope, palpitations, bradycardia, atrial fibrillation, myocardial infarction, cardiac arrest, arrhythmia, and ventricular ectopic activity, including ventricular tachycardia (see **WARNINGS**).

OVERDOSAGE

Animal Oral LD_{50}

The oral LD_{50} of the drug is 610 mg/kg in mice, 486 mg/kg in rats, and 560 mg/kg in rabbits.

Signs and Symptoms
Death from overdose has occurred in patients ingesting DESYREL (trazodone hydrochloride) and other drugs concurrently (namely, alcohol; alcohol + chloral hydrate + diazepam; amobarbital; chlordiazepoxide; or meprobamate).
The most severe reactions reported to have occurred with overdose of DESYREL alone have been priapism, respiratory arrest, seizures, and EKG changes. The reactions reported most frequently have been drowsiness and vomiting. Overdosage may cause an increase in incidence or severity of any of the reported adverse reactions (see **ADVERSE REACTIONS**).

Treatment
There is no specific antidote for DESYREL. Treatment should be symptomatic and supportive in the case of hypotension or excessive sedation. Any patient suspected of having taken an overdose should have the stomach emptied by gastric lavage. Forced diuresis may be useful in facilitating elimination of the drug.

DOSAGE AND ADMINISTRATION
The dosage should be initiated at a low level and increased gradually, noting the clinical response and any evidence of intolerance. Occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime or a reduction of dosage. DESYREL should be taken shortly after a meal or light snack. Symptomatic relief may be seen during the first week, with optimal antidepressant effects typically evident within two weeks. Twenty-five percent of those who respond to DESYREL require more than two weeks (up to four weeks) of drug administration.

Usual Adult Dosage
An initial dose of 150 mg/day in divided doses is suggested. The dose may be increased by 50 mg/day every three to four days. The maximum dose for outpatients usually should not exceed 400 mg/day in divided doses. Inpatients (ie, more severely depressed patients) may be given up to but not in excess of 600 mg/day in divided doses.

Maintenance
Dosage during prolonged maintenance therapy should be kept at the lowest effective level. Once an adequate response has been achieved, dosage may be gradually reduced, with subsequent adjustment depending on therapeutic response.
Although there has been no systematic evaluation of the efficacy of DESYREL beyond six weeks, it is generally recommended that a course of antidepressant drug treatment should be continued for several months.

HOW SUPPLIED
DESYREL® (trazodone hydrochloride)
The 50 mg tablets are white, round, scored tablets debossed with PLIVA;433. They are available as follows:
NDC 68387-165-60
bottles of 60 tablets

Storage
Store at room temperature. Protect from temperatures above 104°F (40°C).
Dispense in tight, light-resistant container (USP).

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DESYREL® (Trazodone Hydrochloride) TABLETS
Medication Guide

About Using Antidepressants in Children and Teenagers

What is the most important information I should know if my child is being prescribed an antidepressant?

Parents or guardians need to think about 4 important things when their child is prescribed an antidepressant:

1. There is a risk of suicidal thoughts or actions

2. How to try to prevent suicidal thoughts or actions in your child

3. You should watch for certain signs if your child is taking an antidepressant

4. There are benefits and risks when using antidepressants

1. There is a Risk of Suicidal Thoughts or Actions

Children and teenagers sometimes think about suicide, and many report trying to kill themselves.

Antidepressants increase suicidal thoughts and actions in some children and teenagers. But suicidal thoughts and actions can also be caused by depression, a serious medical condition that is commonly treated with antidepressants. Thinking about killing yourself or trying to kill yourself is called *suicidality* or *being suicidal*.

A large study combined the results of 24 different studies of children and teenagers with depression or other illnesses. In these studies, patients took either a placebo (sugar pill) or an antidepressant for 1 to 4 months. ***No one committed suicide in these studies***, but some patients became suicidal. On sugar pills, 2 out of every 100 became suicidal. On the antidepressants, 4 out of every 100 patients became suicidal.

For some children and teenagers, the risk of suicidal actions may be especially high. These include patients with

- Bipolar illness (sometimes called manic-depressive illness)

- A family history of bipolar illness

- A personal or family history of attempting suicide

If any of these are present, make sure you tell your healthcare provider before your child takes an antidepressant.

2. How to Try to Prevent Suicidal Thoughts and Actions

To try to prevent suicidal thought and actions in your child, pay close attention to changes in her or his moods or actions, especially if the changes occur suddenly. Other important people in your child's life can help by paying attention as well (eg, your child, brothers and sisters, teachers, and other important people). The changes to look out for are listed in Section 3, on what to watch for.

Whenever an antidepressant is started or its dose is changed, pay close attention to your child.

After starting an antidepressant, your child should generally see his or her healthcare provider:

- Once a week for the first 4 weeks

- Every 2 weeks for the next 4 weeks

- After taking the antidepressant for 12 weeks

- After 12 weeks, follow your healthcare provider's advice about how often to come back

- More often if problems or questions arise (see Section 3)

You should call your child's healthcare provider between visits if needed.

3. You Should Watch For Certain Signs if Your Child is Taking an Antidepressant

Contact your child's healthcare provider ***right away*** if your child exhibits any of the following signs for the first time, or if they seem worse, or worry you, your child, or your child's teacher:

- Thoughts about suicide or dying

- Attempts to commit suicide

- New or worse depression

- New or worse anxiety

- Feeling very agitated or restless

- Panic attacks

- Difficulty sleeping (insomnia)

- New or worse irritability

- Acting aggressive, being angry, or violent
- Acting on dangerous impulses
- An extreme increase in activity and talking
- Other unusual changes in behavior or mood

Never let your child stop taking an antidepressant without first talking to his or healthcare provider. Stopping an antidepressant suddenly can cause other symptoms.

4. There are Benefits and Risks When Using Antidepressants

Antidepressants are used to treat depression and other illnesses. Depression and other illnesses can lead to suicide. In some children and teenagers, treatment with an antidepressant increases suicidal thinking or actions. It is important to discuss all the risks of treating depression and also the risks of not treating it. You and your child should discuss all treatment choices with your healthcare provider, not just the use of antidepressants.

Other side effects can occur with antidepressants (see section below).

Of all antidepressants, only fluoxetine (Prozac®) has been FDA approved to treat pediatric depression.

For obsessive compulsive disorder in children and teenagers, FDA has approved only fluoxetine (Prozac®), sertraline (Zoloft®), fluvoxamine, and clomipramine (Anafranil®).

Your healthcare provider may suggest other antidepressants based on the past experience of your child or other family members.

Is this all I need to know if my child is being prescribed an antidepressant?

No. This is a warning about the risk for suicidality. Other side effects can occur with antidepressants. Be sure to ask your healthcare provider to explain all the side effects of the particular drug he or she is prescribing. Also ask about drugs to avoid when taking an antidepressant. Ask your healthcare provider or pharmacist where to find more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Prozac® is a registered trademark of Eli Lilly and Company

Zoloft® is a registered trademark of Pfizer Pharmaceuticals

Anafranil® is a registered trademark of Mallinckrodt Inc.

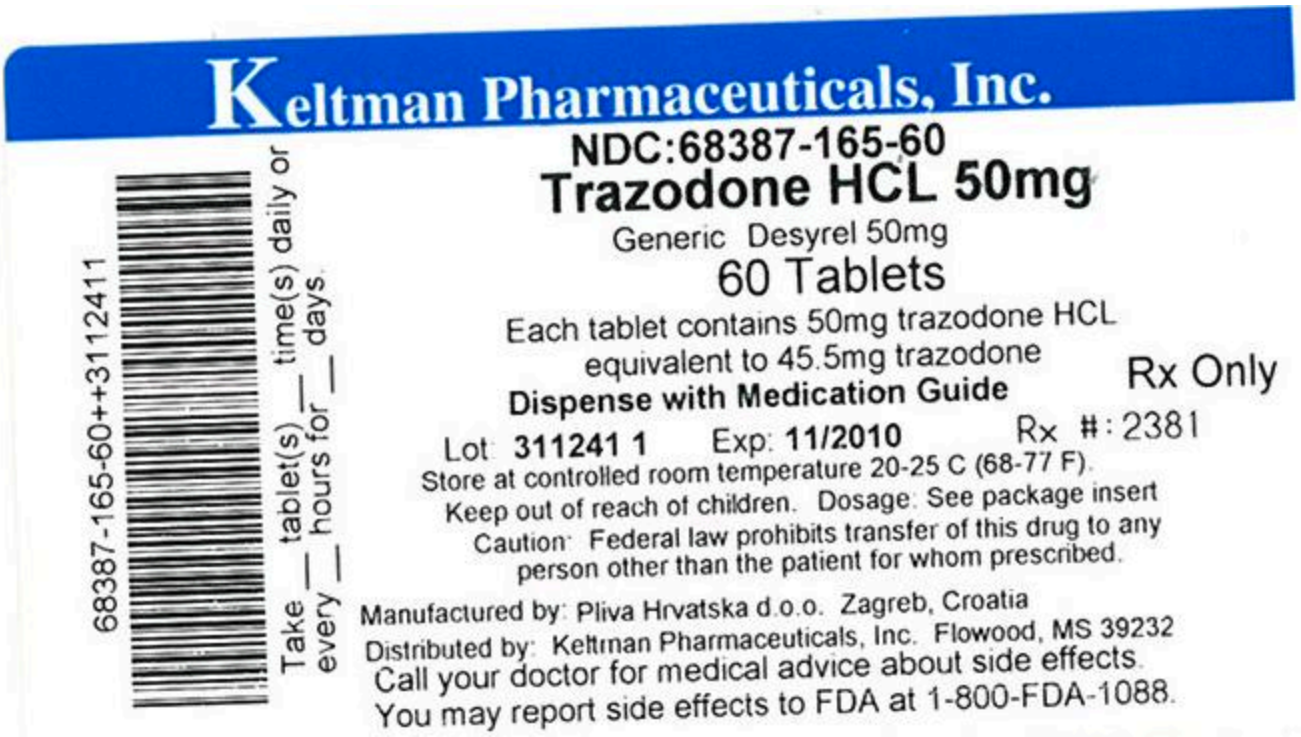
This Medication Guide has been approved by the U. S. Food and Drug Administration for all antidepressants.

Manufactured for:
Keltman Pharmaceuticals Inc.
1 Lakeland Square, Suite A
Flowood, Ms 39232
R4

Package Label - Principal Display Panel – 60-count Bottle, 50 mg Tablets

NDC 68387-165-60

Rx Only



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